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REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons which follow.

A. Response to Objection to Sequence Listing As New Matter.

The Examiner has maintained an objection to the Sequence Listing provided by amendment on January 11, 2002, as introducing new matter into the application. The basis for the objection is that it cannot be determined whether the sequences set forth in the Sequence Listing are the same as those set forth in the original specification, as Figures 1-6, which are contended to be too "illegible, unreadable, and indecipherable" to be understood.

Applicants respectfully maintain that the original Figures, while not in formal form, are sufficiently clear to enable one of ordinary skill in the art to read and understand them. If the identity of any element of the Figures was in doubt, its identity could be readily confirmed by reference to readily available information concerning the known sequences for the *Drosophilia* Sog gene and protein, from which the claimed molecules are derived. The structure of the claimed molecules with respect to the wild-type Sog molecule are, of course, clearly described in the application (see, for example, the Specification at page 3, line 1, specifying that Super-Sog consists of amino acids 1-292 of Sog). Thus, one of ordinary skill in the art could readily identify the sequences depicted in the Figures.

However, because the Figures and Sequence Listing are not essential to an understanding of the invention, but were included only for the convenience of the reader, both have been deleted from the application to allow it to proceed to issue without further delay.

The Specification has been amended accordingly, to delete references to SEQ.ID. Nos. and Figure references. Page 3 of the Specification has been further amended as

summarized below to identify the characteristics of the Super-Sog molecules described within the first paragraph, without need for reference to subsequent pages of the disclosure.

No new matter is added by these amendments, which are supported in the original specification as follows:

- Page 3, line 1: The invention therefore provides Super-Sog (amino acids 1-292 of Sog)...". **Support for the reference to amino acids 1-292 is found in the original disclosure, at page 3, line 1.** ***In view of the deletion of SEQ.ID.No. 1, Claim 1 has also been amended to refer to Super-Sog as consisting of amino acids 1-292 of Sog.***
- Page 3, lines 3-4: "...a Super-Sog peptide which includes a mutation (W→A) at residue 105 in the CR-1 sequence...". **Support for the reference to the mutation being located at residue 105 is found in the original disclosure in original Figure 3, which identifies the mutation by the common symbol of an asterisk beneath the single altered residue, clearly identifiable as being a part of the CR-1 sequence, and located at residue 105 on the Figure.**
- Page 3, lines 5-6: "...a Super-Sog peptide which terminates 5' of the CR-1 sequence at residue 346." **Support for the reference to the termination being located at residue 346 is found in the original disclosure in original Figure 4, which identifies the termination by a clearly identifable STOP notation; as well as at original page 4, lines 5-6, and page 21, lines 21-22, which identify the modified terminus as being 5' of the NotI restriction site.**

Entry of the amendments, and withdrawal of the objections to the now deleted Sequence Listing and Figures, as well as the related rejections of Claims 1 and 2, are requested.

B. Response to Rejections of Claims 1 and 2 As Being Supported by New Matter.

Claims 1 and 2 have been rejected under §112, first paragraph, on the same grounds set forth with respect to the objection to the drawings.

As noted above, those of ordinary skill in the art were quite familiar with the polynucleotide coding sequence for, and polypeptide sequence of, the *Drosophilia* Sog protein, which was published to the art nearly four years before the present application was filed. So too were those of ordinary skill familiar with the structure of the various regions and domains of the Sog gene and protein including, in particular, the CR-1 region from which the claimed Super-Sog derives. See, e.g., Francois, *et al., Genes & Dev.*, 8:2602-2616, 1994; and Specification at page 5, lines 5-24. The invention lies in the discovery that a peptide comprising the first 292 residues of the known Sog protein possessed TGF-beta family growth factor inhibitory activity at least as great as that possessed by full-length, wild-type Sog. Specification at page 5, lines 17-24.

The invention as claimed, therefore, is completely enabled by the foregoing portions of the Specification, which collectively teach that one can use a 1-292 fragment of Sog as a potent TGF-beta family growth factor inhibitor. Those of ordinary skill in the art need be told no more to practice the invention.

It is axiomatic that one need not "inform the layman nor disclose what the skilled already possess" to enable those of ordinary skill in an art to practice an invention. *GENERAL ELECTRIC COMPANY v. BRENNER*, 407 F.2d 1258; 1968 U.S. App. LEXIS 5139; 159 U.S.P.Q. 335 (DC Circuit, 1968). Here, this means that Applicants do not need to reiterate or even incorporate by reference the full-length sequences for Sog already known to the art, but only to define that portion of those known sequence that shall be used in the claimed invention[1]. That they have done.

Applicants therefore request that the rejection of Claims 1 and 2 under §112, first paragraph, be withdrawn.

[1] The Specification's identification of the Francois, *et al.* reference as being one of the many references which identify the Sog coding sequence was all that is required for incorporation of the sequences by reference into the application; no other "magic words" concerning the incorporation are required. *In re de Seversky*, 177 USPQ 144 (CCPA 1973); MPEP 608.01(p). Nonetheless, because Applicants are not required to teach what is already known to those of ordinary skill in the art, the incorporation of Francois, *et al.* into the Specification was not essential to enablement.

C. Response to Rejection of Claim 1 as Incorporating New Matter.

Claim 1 is rejected under §112, first paragraph on the basis that the term "synthetic polynucleotide," as used in the claim, is not set forth in the Specification. Applicants note that the claimed invention is a polynucleotide having the characteristics defined by the claim, which comprise the invention. Applicants are entitled to protection for that invention, regardless of which method of manufacture might be employed to produce it. Synthesis being a well-known process--as acknowledged by the citation of the Maniatis work at page 4 of the Office Action--Applicants hardly need to explicitly suggest it as an option for manufacture of the claimed polynucleotide to those of ordinary skill in the art to demonstrate Applicants' possession of the polynucleotide as produced by such a conventional technique.

However, for purposes of concluding prosecution without further delay, and in recognition that any "synthetic" polynucleotide would necessarily also be isolated and/or purified as specified in the claims, Applicants have amended claim 1 to delete the redundant reference to the term "synthetic." Withdrawal of the rejection of Claim 1 under §112, first paragraph, is therefore requested.

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CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if there are any questions or comments concerning this amendment, or if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 1-8-03

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MARKED UP VERSION SHOWING CHANGES MADE

Below are the marked up replacement paragraph(s) in the Specification.

Page 3, paragraph starting at line 1, is deleted:

[The invention therefore provides Super-Sog (SEQ.ID.No. 1; amino acids 1-292 of Sog) and active variants thereof. Such variants include SEQ.ID.No. 3, a recombinant Super-Sog peptide which includes 33 amino acids encoded by the pUAS expression vector; SEQ.ID.No. 6, a Super-Sog peptide which includes a mutation (W6A) in the CR-1 sequence; and SEQ.ID.No. 7, a Super-Sog peptide which terminates 5' of the CR-1 sequence. Such variants also include Super-Sog with 5' modifications, such as modifications to the Tolloid protease cleavage site, addition of other peptides and inclusion of additional 5' regions of Sog (e.g., CR-2).]

And is substituted to read:

-- The invention therefore provides Super-Sog (amino acids 1-292 of Sog) and active variants thereof. Such variants include a recombinant Super-Sog peptide which includes 33 amino acids encoded by the pUAS expression vector; a Super-Sog peptide which includes a mutation (W→A) at residue 105 in the CR-1 sequence; and a Super-Sog peptide which terminates 5' of the CR-1 sequence at residue 346. Such variants also include Super-Sog with 5' modifications, such as modifications to the Tolloid protease cleavage site, addition of other peptides and inclusion of additional 5' regions of Sog (e.g., CR-2). --

Page 5, paragraph starting at line 6, is amended as follows:

CR-1 is located immediately after the putative transmembrane domain of the Sog protein [(Fig. 1)], while CR-2 through CR-4 are located closer to the coding region for the carboxyl terminus of the protein [(Fig. 6)].

Page 5, paragraph starting at line 13, is deleted:

[Given their similarity in structure, it would be reasonably expected that any *Dpp* inhibitory activity conferred on the Sog protein by the CR repeats would be comparable in quality. It was therefore a surprise to find that a peptide encoded by CR-1 (Super-Sog; SEQ.ID.No.1) has greater Dpp inhibitory activity in certain respects than wild-type Sog.]

And is substituted to read:

-- Given their similarity in structure, it would be reasonably expected that any *Dpp* inhibitory activity conferred on the Sog protein by the CR repeats would be comparable in quality. It was therefore a surprise to find that a peptide encoded by CR-1 (Super-Sog) has greater Dpp inhibitory activity in certain respects than wild-type Sog. --

Page 6, starting at line 16, is deleted:

[Super-Sog is prepared as a purified peptide fragment from Sog (e.g., SEQ.ID.No. 2), expressed as a recombinant peptide using, for example, the coding sequences set forth in SEQ.ID.Nos. 1, 3, 6 or 7, or synthesized chemically. Techniques for production of peptides according to each of these methods are well-known in the art and so will only be described briefly here.]

And is substituted to read:

-- Super-Sog is prepared as a purified peptide fragment from Sog, expressed as a recombinant peptide using, for example, the coding sequences for amino acids 1-292 of Sog, or synthesized chemically. Techniques for production of peptides according to each of these methods are well-known in the art and so will only be described briefly here. --

Page 7, paragraph starting at line 14, is deleted:

[Recombinant Super-Sog can also be produced *in vitro* or *in vivo* through expression of a polynucleotide sequence which encodes Super-Sog (e.g., SEQ.ID.No. 1). In general, prokaryotes are used for cloning of DNA sequences in constructing recombinant expression vectors. For example, *E. coli* K12 strain 294 (ATCC Accession No. 31446) may be particularly useful. Prokaryotes also are used for expression. The aforementioned strain, as well as *E. coli* W3110 (ATTC Accession No. 27325), bacilli such as *Bacillus subtilus*, and other enterobacteriaceae such as *Salmonella typhimurium* or *Serratia marcescans*, and various *pseudomonas* species may also be used for expression.]

And is substituted to read:

-- Recombinant Super-Sog can also be produced *in vitro* or *in vivo* through expression of a polynucleotide sequence which encodes Super-Sog. In general, prokaryotes are used for cloning of DNA sequences in constructing recombinant expression vectors. For example, *E. coli* K12 strain 294 (ATCC Accession No. 31446) may be particularly useful. Prokaryotes also are used for expression. The aforementioned strain, as well as *E. coli* W3110 (ATTC Accession No. 27325), bacilli such as *Bacillus subtilus*, and other enterobacteriaceae such as *Salmonella typhimurium* or *Serratia marcescans*, and various *pseudomonas* species may also be used for expression. --

The Brief Description of Drawings starting at page 3, line 5, and ending on page 4, at line 11, is deleted.

Page 20, paragraph beginning at line 6, is amended as follows:

Wild-type Sog antagonizes Dpp to block wing formation (phenotype 1). For comparison, a broader spectrum vertebrate BMP-4 antagonist (noggin) which shares a fairly high degree of coding sequence homology with Super-Sog [(FIG. 3)] blocks some wing formation (phenotype 1), shortens the distance between wing veins through fusion (phenotype 3) and produces shorter wings (phenotype 4) in *Drosophilia*.

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Below are the marked up amended claim(s).

1. (Twice Amended) An isolated[,] or purified [or synthetic] polynucleotide [comprising the nucleotide sequence of SEQ ID No. 1] encoding amino acids 1-292 of the *Drosophilia* Sog protein.